YALE UNIVERSITY SCHOOL OF MEDICINE
AFFILIATED WITH THE NEW HAVEN HOSPITAL ON THE
ANTHONY N. BRADY MEMORIAL FOUNDATION

DEPARTMENT OF BACTERIOLOGY

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NEW HAVEN, CONNECTICUT

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Dr. Joshua Lederberg
Department of Genetics
University of Wisconsin
Madison, Wisconsin

Dear Josh:

I would like to thank you for the reprints which you sent; also for the earlier series. I hope you will continue to keep me on your list.

We have recently run into one phenomenon which may be of interest to you. In the course of some determinations of mutation rates we ran E. coli No. 58-278 which requires biotin and phenylalanine (I believe this was one of your isolations) against 100 units of streptomycin. With all other strains, including 58 and the wild K-12, and a biotin-methionine-, we obtain growth in about one third of the tubes tested, which give mutation rates of around 3×10^{-10}. Strain 58-278 gave growth in all tubes however. When we plated out cultures on complex medium with and without 100 units of streptomycin, we obtained counts for 58-278 of the order of 1,000,000 to 1; i. e., a tenth ml. of undiluted culture gave 20 to 100 colonies per plate on 100 units of streptomycin.

No other culture tested will give any colonies under these conditions. If this strain is diluted to about 10 organisms per ml. and a series of independent cultures started in broth, and these all allowed to grow out fully, comparative plate counts of each culture with and without streptomycin indicate the presence of about one resistant organism per one million normal forms in every tube. The mutation rate to resistance is thus very high in this culture. It is normal, however, in both the immediate parent, No. 58, and also in a triple mutant biotin-phenylalanine-cystine- (Y-24) which I understand was derived from 58-278. We

could find no evidence of a high mutation rate to resistance with any of five phenylalanine cultures obtained from Davis, so that it is not likely that this high mutation rate is necessarily associated with the phenylalanine locus. This is further indicated by the fact that recombination of 58-278 with a threonine-leucine-B_1- gave prototrophs of which we have now tested 24 colonies out of the 100 found. All 24 colonies when plated out on media with and without streptomycin gave comparative counts similar to those noted above for 58-278. We are naturally continuing work on this strain.

Sincerely yours,

Peter

HPT:EP

Henry P. Treffers
Professor of Microbiology